When people get depressed their brains react in different ways: Knowing this has implications in how best to help them

Predispositions: Genomic; Neuroticism; Negativity Bias; Stress

Hyperprocessing

- Anxious Depression
  - EEG Beta
  - Nonconscious ERP automatic bias to emotion processing
  - Startle EMG
  - ANS Arousal
  - Right Hemisphere
  - fMRI – Amygdala – ACC – Medial – Frontal Cortex

No Adaptive Compromise

- Mixed
  - EEG Coherence measures
  - Variability of all responses
  - Emotion Regulation
  - Symmetry
  - fMRI – Amygdala – ACC – Medial – Frontal Cortex

Hypoprocessing

- Melancholic Depression
  - EEG Theta: Alpha
  - Conscious ERP emotion processing
  - Motor response speed
  - Memory, attention, planning
  - ANS Arousal
  - Left Hemisphere
  - MRI Hippocampus volume – Lateral Frontal Cortex

Clinical

- Limbic – Cortical Tone: SSRI

The Texas Algorithm and STAR-D

Builds on the best algorithms and enhances them
BRC advantages at step one

- Initial drug selection in STAR-D is just citalopram in the Texas Algorithm it could be SSRIs, Bupropion SR, Venlafaxine XR, Mirtazapine, or Nefazadone, but there is no guidance for selection of a particular agent.

- Treatment success at the first step is less than 50% with high drop out rates and non-adherence.

- Using web based neuropsychology tests backed by an integrated database which is normed and age and education matched to create better understanding of the probable endophenotype at a personalized level, while not yet able to produce the “absolute certainty” of personalized medicine at an individual level for a specific agent can significantly increase the likelihood of a successful step one match increasing the chance of a faster more acceptable response, greater adherence and decreased costs from possibly avoidable switching or augmentation.

- In this regard BRC is complimentary to the Texas Algorithm AND makes it even more useful by creating an easy to use decision support for step one.
The iSPOT-A trial is the largest study to date focused on identifying Gene-Brain-Cognition Biomarkers for ADHD and predicting treatment response in ADHD.

| Baseline Assessment | Diagnostic interview and clinical workup  
Symptom ratings  
Web self report (functional status, stress, traits)  
Genomics (saliva)  
Touchscreen (General & Emotional Cognition tasks)  
Brain function (EEG, MRI) |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Treatment</td>
<td>Treatment with stimulant medication (short-acting Methylphenidate)</td>
</tr>
</tbody>
</table>
| On-treatment Assessment at Week 6 | Symptom ratings (Conner’s Rating Scale)  
Web self report (functional outcome, stress, traits)  
Touchscreen (General & Emotional Cognition tasks)  
Brain function (EEG, MRI) |
| Weeks 24 and 52     | ADHD Clinical Monitoring  
Symptom ratings  
Assessing remission and recovery |
### International Study to Predict Optimized Treatment in Depression (iSPOT-D)

The iSPOT-D trial is the largest study to date focused on identifying Gene-Brain-Cognition Biomarkers for Major Depressive Disorder (MDD) and predicting treatment response in MDD.

| Baseline Assessment | Diagnostic interview and clinical workup  
|                     | Symptom ratings  
|                     | Web self report (functional status, stress, traits)  
|                     | Genomics (blood)  
|                     | Touchscreen (General & Emotional Cognition tasks)  
|                     | Brain function (EEG, fMRI)  
|                     | Brain structure (MRI, DTI) |

### Randomization to treatment
MDD randomized to one of 3 medications; Escitalopram, Sertraline or Venlafaxine

| Weeks 1, 2, 4 and 6 | MDD Clinical Monitoring  
|                     | Symptom ratings  
|                     | Assessing ‘placebo’ and initial treatment response |

| On-treatment Assessment at Week 8 | Symptom ratings  
|                                 | Web self report (functional outcome, stress, traits)  
|                                 | Touchscreen (General & Emotional Cognition tasks)  
|                                 | Brain function (EEG, fMRI) |

| Weeks 12, 16, 24 and 52 | MDD Clinical Monitoring  
|                         | Symptom ratings  
|                         | Assessing remission and recovery |
Example of use of BR methodology
Is a change clinically meaningful?

The Database provides a frame of reference for better quantification of the effectiveness of a particular compound.

Drug X may cause a significant change in the DV, however only drug Y shows a change that is clinically meaningful.

**Drug X** $(p < .05)$

**Drug Y**
But can we leverage the new neuroscience to go beyond brain sickness into brain health?
Neurogenesis

Why are we so reluctant to incorporate the implications?
The Implications of a Brain that can change itself.

Can we train and develop the emotional brain as well as we do the cognitive brain?

In an age of knowledge workers could this hold the competitive edge?
**Cajal:** At the start of the 20th century Cajal proposed that brain cells—unlike every other cell in our body—don’t divide. They don’t die, and they are never reborn. **We emerge from the womb with the only brain we will ever have.**

**Pasko Rakic,** the chairman of Yale University’s neurobiology department was the most convincing modern defender of this theory. “All neurons of the rhesus monkey brain are generated during pre-natal and early post-natal life,” Rakic wrote in his 1985 paper, “Limits of Neurogenesis in Primates.” “**Not a single**” new neuron “**was observed in the brain of any adult animal.**”
Fernando Nottebohm

Showed that songbirds, in order to survive and create new songs, added at least 1% of new tissue to their song centers each day.
Are New Neurons Formed in the Brains of Adult Mammals?

In an autoradiographic investigation, the production of brain lesions in rats was combined with intracranial injection of thymidine-H3. In addition, some neurons and neuroblasts showed labeling, suggesting the possibility of proliferation of neurons in adult rats.

Michael Kaplan: 1977 The University of New Mexico

MITOTIC NEUROBLASTS IN THE 9-DAY-OLD AND 11-MONTH-OLD RODENT HIPPOCAMPUS

MICHAEL S. KAPLAN AND DANNY H. BELL

Department of Anatomy, University of New Mexico School of Medicine, Albuquerque, New Mexico 87131

...The electron microscopic observations reported in this study reveal: (1) that a steady rate of granule cell neurogenesis occurs during the first year of a rodent's life; (2) that newly formed granule neurons in the dentate gyrus of the newborn mouse and adult rat are a result of neuroblast division; and (3) two distinct classes of mitotic cells can be identified during the peak period of postnatal neurogenesis - those with synapses on their cell bodies and processes and those with no synapses or processes.

Rakic told him “They may look like neurons in New Mexico but they don’t in New Haven”
In 1989 Gould while looking at rat brain degeneration in rats following glucocorticoid administration found that the brain also healed itself.
In December 2000 published a paper in the *Journal of Neuroscience* demonstrating that antidepressants increased neurogenesis in the adult rat brain. In fact, the two most effective treatments they looked at—electroconvulsive therapy and Prozac increased neurogenesis in the hippocampus by 75% and 50%, respectively. Subsequent studies did this by increasing the exact same molecules, especially trophic factors, that are suppressed by stress.

**Luca Santarelli:** Columbia

*Science* 301 (5634): 805-809 2003

**Requirement of Hippocampal Neurogenesis for the Behavioral Effects of Antidepressants**

Luca Santarelli, 1* Michael Saxe, 1* Cornelius Gross, 1 Alexandre Surget, 2 Fortunato Battaglia, 3 Stephanie Dulawa, 1 Noelia Weisstaub, 1 James Lee, 1 Ronald Duman, 4 Ottavio Arancio, 3 Catherine Belzung, 2 René Hen 1.

…….. Here, using genetic and radiological methods, we show that disrupting antidepressant-induced neurogenesis blocks behavioral responses to antidepressants
A new paradigm

The partially developed brain

The developed healthy brain

The breaking stressed brain

Every day your cognitive brain is hostage to your emotional brain
Nutrition, Exercise and the Brain

- Stimulation of Cognitive Development
- Prevention of Cognitive Ageing
- Optimization of Cognitive Performance

MENTAL ABILITY
MENTAL PERFORMANCE

Infant | Child | Adult | Elderly

- Optimal development in children
- Optimized performance throughout life
- Prevention of cognitive decline in elderly
Participants were classified into 4 quartiles based on the number of blocks walked, and MRI measurement 9 years later ascertained that gray matter volume in the highest quartile differed from the other 3 quartiles (all \( P < .05 \)). Participants who walked at least 72 blocks — approximately 6 to 9 miles — per week had more gray matter than people who walked less; however, walking more than 72 blocks did not appear to increase gray matter volume any further.

Areas of the brain with an increase in volume associated with a reduced risk of developing cognitive impairment were the inferior frontal gyrus (odds ratio [OR], 1.99; \( P < .01 \)), hippocampal formation (OR, 2.01; \( P < .009 \)), and supplementary motor area (OR, 2.24; \( P < .01 \)).

In the 4-year follow-up, 116 of the participants, or 40%, had developed cognitive impairment or dementia. Greater gray matter volume with physical activity was associated with a 2-fold reduced risk for cognitive impairment.
In Brooklyn a new yoga center that promises to do as much for your grey matter as it does for your skin and bones. The brain & body center promises folks who attend that they can “gain a sense of empowerment over your brain and your body.”

Body & Brain Wellness Center, 130 Clinton Street, Brooklyn, NY 11201
Exercise Improves Brain Power

Exercise and mental stimulation both boost other memory late in life

Physical exercise is known to be good for the aging brain, but what about mental stimulation? Does enrichment that helps older people work well for the young and middle aged, or do they need something else? A report in the August issue of Behavioral Neuroscience tells how, in an enrichment. For the young and middle aged, exercise is key.

Behavioral Neuroscience is published by the American Psychological Association (APA).

Age, exercise may boost memory

Tuesday, November 25, 2003 Posted: 9:59 AM EST (1459 GMT)

(CNN) -- "You're not getting older, you're getting better." New research shows this traditional compliment may be true when it comes to memory, especially for someone who stays in shape.

Recent studies indicate that a simple exercise routine helps put the brakes on memory loss. And one aspect of memory automatically improves with age, according to a new study.

What makes an exercise Neurobic? Through the course of everyday, your brain is activated by your senses.

Physical and Brain Exercise Boost Memory

Researchers at Yale University have just released a good paper showing the importance of both physical and mental exercise to maintain good memory. Their research paper Single Enrichment Variables Reduce Aged-related Decline in Female Mice).
January 26, 2009
Nintendo brain-trainer 'no better than pencil and paper'
The largest trial to date of 'brain-training' computer games suggests that people who use the software to boost their mental skills are likely to be disappointed.

The study, a collaboration between British researchers and the BBC Lab UK website, recruited viewers of the BBC science programme Bang Goes the Theory to practise a series of online tasks for a minimum of ten minutes a day, three times a week, for six weeks. In one group, the tasks focused on reasoning, planning and problem-solving abilities — skills correlated with general intelligence. A second group was trained on mental functions targeted by commercial brain-training programs — short-term memory, attention, visuospatial abilities and maths. A third group, the control subjects, simply used the Internet to find answers to obscure questions. A total of 11,430 volunteers aged from 18 to 60 completed the study, and although they improved on the tasks, the researchers believe that none of the groups boosted their performance on tests measuring general cognitive abilities such as memory, reasoning and learning.

"There were absolutely no transfer effects" from the training tasks to more general tests of cognition, says Adrian Owen, a neuroscientist at the Medical Research Council (MRC) Cognition and Brian Sciences Unit in Cambridge, UK, who led the study. "I think the expectation that practising a broad range of cognitive tasks to get yourself smarter is completely unsupported."

It's unlikely that the study, published online in Nature this week, will quell the brain-training debate. "I really worry about this study — I think it's flawed," says Peter Snyder, a neurologist who studies ageing at Brown University's...
www.MyBrainSolutions.com is a website for self-improvement which draws on new insights to develop better brain habits.
Continuum of Care
Modularized inter-operability and selected Integration

www.mybrainsolutions.com

Self-Paced online Brain Training Solutions

Option with HRA in BRISC

Personal Health Record

Virtual Communication
Tracking and Monitoring
Personalized Outreach

Timely, Accurate Treatment Decisions

Case Scenarios

John Smith: November 18th
Welcome, John!

John's MBS Progress:
Send John a message:

Alert:
New Report from patient

Message from John Smith
Disclaimer

This report provides indications of general cognition and social cognition as compared directly or indirectly to a normative database. It is not to be used as a basis for action without consideration by a competent relevant professional. Always seek the advice of a trained health professional or relevant specialist regarding any highlighted variances within this report before any treatment or action is taken. This report is not intended to be used in any way on its own to diagnose, select treatment or cure any health condition. This report does not establish any physician-patient relationship or supplant any in-person medical consultation or examination. Appropriate medical attention should always be sought for specific ailments. Do not disregard professional medical advice or delay seeking medical treatment as a result of findings contained within this report. Brain Resource expressly disclaims any and all responsibility for any liability, loss or risk which may be or is incurred as a consequence, directly or indirectly, of any use and application of this report.
Welcome, John!

Know – Train – Optimize Your Brain
Educate, Motivate, Set Goals

- Know Your Brain
  - Know
  - Train
  - Optimize

- Goal Setting
  - Specific
  - Measurable
  - Attainable
  - Realistic
  - Time bound

- Communication
  - Focus
  - Engage
  - Opinion
  - Position
  - Storytelling

- MyCalmBeat
  - Breathe at Your Best Breathing Rate to reduce stress and enhance focus

- Brain Exercise
  - Interval Training for Brain Health

- EQ (Emotional Intelligence)
  - Align your Emotions & Thinking

- Insomnia Relief
  - Better sleep hygiene

- Brain - Body
  - Stress - Recovery
  - Growth
  - Stress

- Brain Nutrition
  - Overcoming Emotional Eating

30
Applying the INTEGRATE Model

The brain is highly interconnected: Train 1  Effect All
Thinking Training Example

e-Think Executive

LEVEL: 3
SCORE: 1,388

GAMES PLAYED: 2

TIME REMAINING: 38 seconds
Not just a rich knowledge base, but smart tools and programs for assessment, online cognitive therapy, journaling, coaching and prevention. Embedded screening logic - tools adjust to member response.
Heart Rate Variability—The Connection

- You have a personalized **BEST BREATHING RATE**, or **Resonant Frequency**, where your body is aligned for peak performance.
- When you are breathing at your Resonant Frequency, your heart and brain are working together in synchrony and you are **calm**, **focused** and **“in the zone”**.
## Polyvagal Theory: Phylogenetic Stages of Neural Control

<table>
<thead>
<tr>
<th>Stage</th>
<th>ANS Component</th>
<th>Behavioral Function</th>
<th>Lower motor neurons</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>Myelinated vagus <em>((VVC – ventral vagal complex))</em></td>
<td>Social communication, self-soothing and calming, inhibit sympathetic-adrenal influences</td>
<td>Nucleus ambiguus</td>
</tr>
<tr>
<td>II</td>
<td>Sympathetic-adrenal system <em>((SNS – sympathetic nervous system))</em></td>
<td>Mobilization (active avoidance)</td>
<td>Spinal cord</td>
</tr>
<tr>
<td>I</td>
<td>Unmyelinated vagus <em>((DVC – dorsal vagal complex))</em></td>
<td>Immobilization (death feigning, passive avoidance)</td>
<td>Dorsal motor nucleus of the vagus</td>
</tr>
</tbody>
</table>
But Heart Rate Variability (HRV) also is a Measure of Adaptive Capacity

- Higher HRV
  - Survival in neurosurgery
  - Youth (age <40)
  - Aerobic fitness
  - Exercise/altitude tolerance
  - Better neurocognitive executive function

- Lower HRV
  - Heart failure
    - Disability
  - Death after heart attack
  - Diabetic cardiovascular disease
  - Right atrial hypertrophy in hypertension
  - Depression, anxiety, stress
  - SIDS
  - Febrile state
  - Most diseases
High HRV associated with better performance on tasks involving executive function.

(Hansen, Johnsen, & Thayer, 2003)
Pilot Study: HRV Biofeedback vs Coherent Breathing for Depression

- 11 depressed subjects: 10 weekly sessions train to breathe at resonant frequency for maximal HRV; 20 min 2x/d
- 9/11 significant improvement in depression: effect size 3.6
- Vegetative symptoms improved most with significant improvement by wk 4
- Improvements correlated with ↑ HRV and vagal activity (Karavidas et al. Appl Psychophysiol Biofeedback. 2007)
Low heart rate variability (and faster breathing) has been connected to worry and negative feelings, pain, and stresses at work \[1-3\].

Higher heart rate variability enables people to recover more easily from stress, and boost their positive feelings \[2\].

Higher heart rate variability is also beneficial to our ability to focus and concentrate, and to think clearly \[4\].

2) Thayer J and Lane RD. (2000).
The MyCalmBeat Workshop is appropriate for populations that have high stress environments (i.e., call centers, etc).

1. Representative sets up a whole day or multi-day workshop on-site.

2. On-site internal champion is trained by representative or receives a standalone kit. Internal Champion trains to run Workshops within population.

Employee Receives their Personal Best Breathing Rate (12 minute calculation)

Employee Trains at Personal Best Breathing Rate via MyCalmBeat Exercise on MyBrainSolutions

Employee Registers on www.MyBrainSolutions.com

Employee can train on mobile phone that synchs to exercise on MyBrainSolutions
Cell Phone Applications

MyBrainSolutions
Optimize Yourself
Integrates with MyBrainSolutions

As a registered user of www.mybrainsolutions.com, use the MyCalmBeat tracker on your Dashboard. Set the breathing bar to your Resonant Frequency.
MyCalmBeat objectively calculates your Best Breathing Rate (Resonant Frequency), at which YOU will be most calm and focused.

You train on your cell phone at YOUR rate for 20 minutes a day, prior to any event you need to perform, and at “Critical Moments”.

Applications to stress management, productivity & personal peak performance. Can also be used in applying to pain relief.

**Calculate with Heart Rate Monitor**

**Train by pacing breathing to Personal Rate**
MyCalmBeat Application 2: MyCalmBeat Biofeedback

By Breathing at Your Best Breathing Rate you have increased your Heart Rate Variability by:

88 %

Average Heart Rate: 76 Beats Per Minute

Heart Rate Monitor Battery: 79%
MyCalmBeat Application 3: Interfacing to Games

**e-Self Regulate**

*In this game, master the Self Regulation of your feelings.*

- Remember when you felt **ANXIOUS** (worried, fearful), like this.
- Engage this feeling.
- Notice any breathing or heart beat changes.
- Now – imagine a different outcome, that would make you feel relaxed and calm.
- Press when you’re ready to imagine.
- Press again as soon as you experience a boost in feeling **Calm**.

---

**Breathe OUT**

**SET YOUR BREATHING RATE:**

- **5.5**
  - breaths per minute

---

**Average Heart Rate:**

- **70 Beats Per Minute**

---

**Heart Rate**

- **Average:**
  - **70**
  - **60**
  - **50**
  - **40**
  - **30**
  - **20**
  - **10**
Applying the INTEGRATE Model

The brain is highly interconnected : Train 1       Effect All

Achieve Authentic Happiness
“Cultivate your most fundamental strengths (and virtues) and use them everyday in work, play and parenting” (Martin Seligman 2002).

• Positive Contagion.

Meaning & Purpose
Being a part of something larger than yourself

Strengths & Virtues

Courage
Integrity
Diligence

Wisdom
Learning
Open-minded
EQ
Perspective

Justice
Fairness

Transcendence
Forgiveness
Hope
Spiritual

Temperance
Self-restraint
Humility
Modesty

Humanity
Loving kindness
Gratitude

Optimistic

PAST
Reconcile

PRESENT
Bodily Pleasures
Gratifications (“Flow”)

FUTURE
Brain Points
*Training improves Social Skills

*Training is higher for those who start with lower Social Skills
* Example of Employee use of MyBrainSolutions showing improvement for High and Low amount of Training on Positivity Bias and Emotional Resilience

* This is not a practice effect as no meaningful change is present over time for controls

**STATS:**

<table>
<thead>
<tr>
<th></th>
<th>High Level</th>
<th>Low Level</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positivity Bias</strong></td>
<td>p&lt;.001</td>
<td>Non-Sig.</td>
<td>Non-Sig.</td>
</tr>
<tr>
<td><strong>Social Skills</strong></td>
<td>p&lt;.001</td>
<td>Non-Sig.</td>
<td>Non-Sig.</td>
</tr>
<tr>
<td><strong>Emotional Resilience</strong></td>
<td>p&lt;.001</td>
<td>p&lt;.01</td>
<td>Non-Sig.</td>
</tr>
</tbody>
</table>
How might life be different if we put it together?